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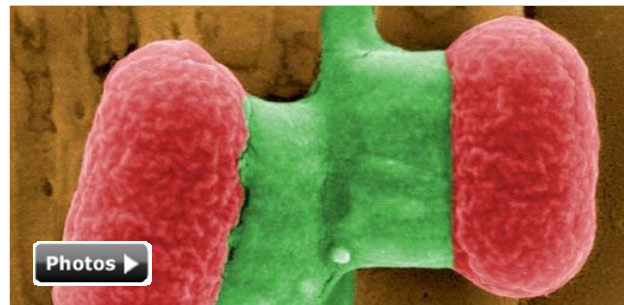
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The Epidemic Detectives

The Hunt for the Source of Germany's E. Coli Outbreak

By Veronika Hackenbroch, Samiha Shafy and Frank Thadeusz



DPA/ HZI/ Manfred Rohde

Germany's E. coli epidemic, which has killed as many as 15 people so far, has alarmed doctors, who have never seen such an aggressive intestinal bacteria before. Epidemiologists are desperately searching for the origin of the deadly bacteria.

The eeriest thing of all, according to Rolf Stahl, is the way patients change. "Their awareness becomes blurred, they have problems finding words and they don't quite know where they are," says Stahl. And then there is this surprising aggressiveness. "We are dealing with a completely new clinical picture," he notes.

Stahl, a 62-year-old kidney specialist, has been the head of the Third Medical Clinic and Polyclinic at the University Medical Center Hamburg-Eppendorf (UKE) for almost 18 years. "But none of us doctors has ever experienced anything quite like this," he says. His staff has been working around the clock for the last week or so. "We decide at short notice who can go and get some sleep."

The bacterium that is currently [terrifying the country](#) is an enterohemorrhagic strain of the bacterium Escherichia coli (EHEC), a close relative of harmless intestinal bacteria, but one that produces the dangerous Shiga toxin. All it takes is about 100 bacteria -- which isn't much in the world of bacteria, which are normally counted by the millions -- to become infected. After an incubation period of two to 10 days, patients experience watery or bloody diarrhea.

'The Situation Is Deteriorating Dramatically'

But Stahl only sees the most severe cases, those in which EHEC also attacks the blood, kidneys and brain. These patients suffer from a life-

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threatening complication known as hemolytic-uremic syndrome (HUS). About 10 days after the diarrhea begins, the red blood cells suddenly disintegrate, blood clotting stops working and the kidneys fail. In many cases patients need dialysis to stay alive.

"The situation is deteriorating dramatically for our patients," says Stahl. "And the worst thing is that we don't know what's causing it."

In Germany, about 60 people a year contract hemolytic-uremic syndrome after being infected with EHEC. Last week, there were as many cases in a single day. According to the Robert Koch Institute (RKI), the national German institution responsible for disease control and prevention, there were 276 HUS patients in German hospitals by Friday.

By Tuesday there were 373 confirmed cases of HUS across Germany. As many as 15 people may have died from EHEC in Germany so far in the current outbreak. Cases have also been reported in Sweden, Denmark, Britain, Austria and the Netherlands. Meanwhile Russia has banned imports of cucumbers, tomatoes and fresh salad from Spain and Germany.

Impressive Detective Work

The story of the outbreak began in Stahl's clinic. When the first patient suspected of having contracted HUS was admitted there on a Wednesday evening two weeks ago, none of the doctors had any idea what they were facing. "We weren't even thinking of EHEC at first," says Stahl, "because it normally only affects children." In adults, on the other hand, HUS can also be caused by genetic defects and autoimmune diseases, or as a side effect of cancer treatment.

By the next day, however, there were suddenly seven or eight cases in the ward, and the laboratory reported that they were all infected with EHEC. Hamburg promptly notified the Robert Koch Institute.

The process that began at that point and reached its preliminary climax at the end of last week with the closing of two vegetable production operations in Spain is an example of impressive epidemiological detective work. It involves close cooperation among vigilant doctors, epidemiologists thinking practically and detail-oriented laboratory scientists.

For the disease control experts at the RKI, it was primarily a matter of addressing two tasks simultaneously and as quickly as possible: to find the contaminated food products and to determine the type of bacterium involved.

Extremely Rare

Helge Karch, the director of the RKI's EHEC consulting laboratory at the Münster University Hospital in western Germany, has devoted almost his entire life as a researcher to EHEC bacteria. "But I've never encountered something like this," he says.

The first stool sample arrived in his lab on Monday. The first cases had already appeared in the state of North Rhine-Westphalia by then.

Karch's staff members began their analysis right away. The result was clear by Wednesday evening: It was the extremely rare serotype O104:H4.

Karch spent a sleepless night in front of his computer. The serotype he had identified was so rare that he had only encountered it once in three decades. But had this bacterium ever triggered an epidemic before?

After searching through a database for medical journals, Karch found only one article under the search term "O104:H4": a case study from Korea. In the Korean case, as in most of the German cases, an adult woman had contracted EHEC, which is completely atypical for EHEC.

Plague DNA

Karch kept himself awake with coffee, and to relax he went for walks with his German shepherd. "Can you imagine what I'm going through?" he wrote in an email to Phillip Tarr at Washington University in St. Louis. His response came at 4:27 a.m.: "Epidemics are for younger men." Tarr, the second major EHEC expert next to Karch, had also never heard of an O104:H4 outbreak.

In the email, Karch speculated over why the disease wasn't happening in children, as is normally the case, but only in adults. And why was the

infection striking more people than ever before in Germany -- so many, in fact, that dialysis stations in several hospitals were almost full?

Karch and others speculate that the problem could lie in the pathogen itself. Perhaps the genetic material of this rare bacterium has mutated again, so that its toxin or its bond to the intestinal cells it damages has become stronger. Doctors hope that a complete sequencing of the genome, which is now being performed in Münster, will offer some answers.

On Tuesday, the German newspaper *Süddeutsche Zeitung* reported that Karch had discovered that the O104:H4 bacteria responsible for the current outbreak is a so-called chimera that contains genetic material from various E. coli bacteria. It also contains DNA sequences from plague bacteria, which makes it particularly pathogenic. There is no risk, however, that it could cause a form of plague, Karch emphasized in remarks to the newspaper.

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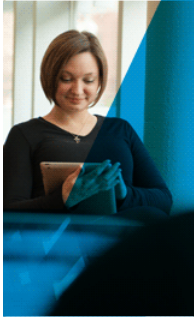
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